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British Journal of Medicine & Medical Research

21(7): 1-10, 2017; Article no.BJMMR.33614
ISSN: 2231-0614, NLM ID: 101570965

Short Term Rehospitalisation or Death and Determinants after Acute Heart Failure Admission in a Cohort of African Patients in Port Harcourt, Southern Nigeria

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Authors' contributions

This work was carried out in collaboration between both authors. Author OI developed the concept of the study, recruited the study subjects, carried out the cardiac procedures, statistical analysis and participated in the development and write up of the manuscript and references. Author MRA participated in conceptualization, performance of the cardiac procedures and the preparation of the manuscript, corrections and references. Both authors read and approved the final manuscript.

Article Information

DOI: 10.9734/BJMMR/2017/33614
Editor(s):
(1) Pietro Scicchitano, Cardiology Department, Hospital "F. Perinei" Altamura (Ba), Italy.
Reviewers:
(1) Bilal Munir, Heart and Vascular Institute, University of Pittsburgh Medical Center, USA.
(2) Franco Mantovan, University of Verona, Italy.
Complete Peer review History: http://www.sciencedomain.org/review-history/19120

Original Research Article

Received 23rd April 2017
Accepted 14th May 2017
Published 18th May 2017

ABSTRACT

Background: Heart failure [HF] is a major health burden globally and contributes significantly to morbidity and mortality related to cardiovascular disease. The aim was to determine the outcome and factors that determine these outcomes of patients admitted for acute HF and followed up for six months.
Methodology: A hospital-based prospective study. Subjects consisted of consecutive patients with confirmed diagnosis of acute HF admitted into the medical wards of the University of Port Harcourt Teaching Hospital [UPTH] in Nigeria over 1 year. All had full physical examination and relevant investigations including echocardiography. Subjects were followed up for six months and

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reassessed for outcome/endpoint which were rehospitalisation or death. Factors that predicted these outcomes were also determined.

Results: There were 160 subjects, 84 females and 76 males, age range 20 to 87 years, mean 52.49±13.89 years. Sixteen (16) subjects (10.0%) were lost to follow up, 66(41.3%) showed improvement clinically, 57(35.6%) were rehospitalised while 21(13.1%) died. Determinants of rehospitalisation were New York Heart Association (NYHA) class, heart failure type, haemoglobin level at presentation and the estimated glomerular filtration rate (e GFR). Determinants of mortality were NYHA class and left ventricular ejection fraction at presentation.

Conclusion: Heart failure rehospitalisation and mortality rates of 35.6% and 13.1% respectively is high compared to developed countries.

Keywords: Heart failure; outcomes; rehospitalisation; mortality.

1. INTRODUCTION

Heart failure (HF) is the end stage of most diseases of the heart and is a major cause of morbidity and mortality. Thomas Lewis aptly captured the high premium placed on HF as far back as 1933 when he remarked, "The very essence of cardiovascular practice is the early detection of heart failure". [1] The worldwide prevalence and incidence rates of HF are approaching epidemic level, as evidenced by the increase in the number of HF hospitalizations, the increasing number of HF-attributable mortalities and morbidity [2,3]. Worldwide, HF affects almost 23 million people [2] and up to three million people in the United Kingdom are affected [4]. The financial burden of HF in most countries is very substantial. In the United States about $30.7 billion was spent directly or indirectly on HF management in 2012 and projected to rise to 69.7 billion dollars by 2030 [5]. The peak incidence of HF in African patients remains in the fifth decade [6] and the hospital case fatality ranges from 9% to 12.5% [7]. This high death rate ranks HF among the major causes of death of cardiovascular origin in Africa [7]. In Port Harcourt, Niger Delta region of Nigeria, HF was the third commonest non communicable cause of admission (next to diabetes and its complications and cerebrovascular disease) and contributed 9.6% of patients admitted to the medical wards over a 5 year period [8-9]. The prognosis of HF is uniformly poor as five year mortality remains high at 50% and factors such as late presentation in advance heart failure, low haemoglobin level and impaired renal function have been identified as contributory factors for this poor outcome [10-16]. The aim of the study was to determine the short term [6 months] outcome and factors that influence these outcomes in patients admitted with acute heart failure in Port Harcourt, Southern Nigeria.

2. METHODOLOGY

The was a hospital-based prospective study carried out in the medical wards of the University of Port Harcourt Teaching Hospital (UPTH), Port Harcourt, Niger Delta region of Nigeria. All the patients admitted into the medical wards with a confirmed diagnosis of acute heart failure [AHF] from 1st January to 31st December 2014 for the first time were recruited. The patients were selected if they met the Framingham [17] clinical criteria for the diagnosis of HF and confirmed on echocardiography. Demographic data was obtained from all patients aged 18-years and above who gave written informed consent. The hospital's ethics committee approved the study. The NYHA functional class, baseline clinical and demographic characteristics of patients were obtained using a structured questionnaire. All study subjects underwent full clinical examination, anthropometric measurements and relevant investigations including chest radiographs, electrocardiograms, and echocardiogram. In addition the list of drugs prescribed on admission was also obtained for all participants.

Blood pressure was measured with a standard mercury sphygmomanometer (cuff size 12.5 X 40 cm) on the patient using standard protocol. Systolic and diastolic blood pressures were taken at korotkoff phases 1 and 5 respectively to the nearest 2 mmHg [18]. An average of two measurements taken 5 minutes apart were recorded and hypertension was deemed present if systolic BP ≥ 140 mmHg and or diastolic BP ≥ 90 mmHg on at least 2 occasions or if patient was receiving anti-hypertensive drug treatment. [18].

Waist circumference was measured in centimeters at the midpoint between the lower costal margin and the iliac crest with the patient

standing and feet positioned close together and the value was read at the end of a normal expiration [19]. Waist circumference was considered increased when it exceeded 88 cm in women and 102 cm in men [19]. Hip circumference was measured in centimeters by the same method as for waist circumference but at the level of the greater trochanter. Waist-hip ratio was calculated by dividing the waist circumference by the hip circumference [19]. Weight was measured with a mechanical weighing scale with the subject wearing only light clothing, and height was measured using a stadiometer with the subject standing feet together without shoes or head gear, and reading taken to the nearest 0.5 cm. Body mass index was calculated using the formula Wt[Kg]/Ht[M]^2. Body mass index status was classified according to the WHO criteria as normal weight (18.5-24.9 kg/m^2), overweight (25–29.9 kg/m^2), class I obesity (30.0-34.9 kg/m^2), class II obesity (BMI 35.0-39.9 kg/m^2), and morbid obesity (BMI ≥ 40 kg/m^2) [19].

Blood samples were collected from all patients and analyzed for haemoglobin, fasting lipid profile, serum urea and creatinine as well as plasma glucose. Serum creatinine was used to calculate the eGFR using the Cockcroft-Gault formula [20]. Severity of renal impairment was classified using the National Kidney Foundation-developed criteria as part of its Kidney Disease Outcomes Quality Initiative (NKF KDOQI) to stratify chronic kidney injury [21]. Fasting serum cholesterol and triglyceride levels were measured using the enzymatic method with a reagent from Atlas Medical Laboratories. Fasting HDL was measured with the precipitation method. LDL cholesterol values were calculated using the Friedwald equation when the triglyceride level was less than 4.0mmol/l: LDL = TC – (HDL + TG /2.2) [22].

Standard 12 lead elctrocardiography was performed for all patients and the parameters assessed in the electrocardiogram included presence of atrial fibrillation, pathological Q waves, left ventricular hypertrophy, QT prolongation and ST abnormalities. The abnormalities on the ECG was deemed to be confirmed if both authors independently agreed to it. Transthoracic echocardiography was performed on all the subjects and assessments were done according to the recommendations of the American Society of Echocardiography [23]. Left Ventricular systolic performance was assessed using the fractional shortening (FS) and the ejection fraction (EF) of the left ventricle. These were calculated automatically by the machine using the Teichoiz formula [24]. The left ventricular mass (LVM) was calculated using the American society of Echocardiography recommended formula for estimation of LV mass from LV linear dimensions [25]. Left Ventricular mass index (LVMI) was calculated by indexing the left ventricular mass to the body surface area. Left ventricular hypertrophy (LVH) was defined in absolute terms as LVMI >115 g/m^2 in men and >95 g/m^2 in women [25]. Left ventricular diastolic function was evaluated by studying the filling dynamics of the left ventricle, the isovolumetric relaxation time (IVRT), the pulmonary venous flow and tissue Doppler imaging derived myocardial wall velocities [26].

2.1 Follow-up

All the study population patients were followed up for 6 months or until death if the patient died before 6 months of follow up. They were assessed during follow up by telephone contacts if they did not keep outpatient appointment. The contact was either patient or next of kin phone contacts and were considered lost contact if telephone contact could not be made after three months of several calls or stated address was not within the city and not traceable in the village documented as residence. The primary end point was death due to any cause and rehospitalization. The duration of follow-up was defined as the interval from the date of the index examination at which the echocardiogram was obtained to the date of death or the date of last contact. During six months follow up, clinical and echocardiographic parameters were obtained and compared with initial values. All the subjects who required readmission had worsening of symptoms and a repeat echocardiographic assessment in all, showed low LV ejection fraction

2.2 Statistical Analysis

Data was analyzed using Statistical Package for Social Sciences (SPSS) version 20.0 Results were presented as mean ± standard deviation for continuous variables while categorical variables were expressed as proportions or percentages. Charts and tables were used to illustrate results where appropriate. Continuous variables were compared by the student's t- test, while proportions or categorical parameters were compared with the chi-square test or two tailed Fisher's exact test. Multiple logistic regression

analysis was done to test associations and a p value of less than 0.05 was considered statistically significant.

3. RESULTS

A total of 160 patients were studied over the study period and were made up of 84 females and 76 males. The age range was 20 to 87 years with a mean of 52.49±13.89 years. A total of 16 subjects (10%) were lost to follow up, 66 subjects (41.3%) improved clinically and continued their regular out-patient clinic attendance for six months, 57 subjects (35.6%) were re hospitalised for worsening of HF symptoms while 21 subjects (13.1%) died. The socio demographic profile of the patients did not have any significant effect on re hospitalisation and mortality. There was significant association between re hospitalisation and NYHA class, type of HF (systolic or diastolic heart failure), body mass index (BMI), haemoglobin level, left ventricular ejection fraction (LVEF) and the eGFR. (Table 1). However when the effects of confounding variables were removed using the logistic regression model, the real determinants of re hospitalisation were the NYHA class, the type of heart failure, the haemoglobin level and the eGFR. (Table 2). There was significant association between mortality and NYHA class, haemoglobin level and LVEF (Table 3). However after logistic regression analysis only the NYHA class and the left ventricular ejection fraction at presentation were the real determinants of mortality (Table 4).

Table 1. Association of different variables with rehospitalisation

Variable	Rehospitalisation			
	No. no (%)	Yes. no (%)	Total no	Chi (p)
Sex				1.033 (0.309)
Male	52 (68.4)	24 (31.6)	76	
Female	51 (60.7)	33 (39.3)	84	
Age group (years)				4.95 (0.084)
18-45	26 (52.0)	24 (48.0)	50	
45-65	56 (70.9)	23 (29.1)	79	
>65	21 (67.7)	10 (32.3)	31	
LOE				0.24 (0.623)
None and Primary	29 (67.4)	14 (32.6)	43	
Secondary/Tertiary	74 (63.2)	43 (36.8)	117	
NYHA class at presentation				26.64 (<0.001)
Class 2	39 (90.7)	4 (9.3)	43	
Class3	44 (47.8)	48 (52.2)	92	
Class 4	20 (80.0)	5 (20.0)	25	
Type of HF				6.05 (0.014)
DHF	14 (93.3)	1 (6.7)	15	
SHF	89 (61.4)	56 (38.6)	145	
BMI (Kg/m^2)				11.72 (0.003)
≤24.99	34 (64.2)	19 (35.8)	53	
25-29.99	35 (52.2)	32 (47.8)	67	
≥30	34 (85.0)	6 (15.0)	40	
Haemoglobin (gm)				5.51 (0.019)
≥10	84 (69.4)	37 (30.6)	121	
<10	19 (48.7)	20 (51.3)	39	
LVEF (%)				7.52 (0.023)
≥40	48 (77.4)	14 (22.6)	62	
25-39.99	40 (56.3)	31 (43.7)	71	
<25	15 (55.6)	12 (44.4)	27	
cGFR (mls/min)				11.17 (0.001)
≥60	76 (73.8)	27 (26.2)	103	
<60	27 (47.4)	30 (52.6)	57	

*Key: LOE=Level of education; NYHA= New York Heart Association; DHF= diastolic heart failure; SHF= systolic heart failure; BMI= body mass index; LVEF= Left ventricular ejection fraction; eGFR= estimated glomerular filteration rate; No= number; %= percent within variable; * = significant p value*

Table 2. Result of logistic regression analysis of some variables with rehospitalisation

	Sig. P value	Odds ratio
NYHA class 2	.000	
NYHA class 3	.271	2.778
NYHA class 4	.000	16.763
Type of HF	.032	15.041
BMI < 24.99	.410	
BMI 25- 29.9	.812	1.171
BMI >>30.0	.285	1.886
HB <10.0gm%	.012	4.187
EF>> 40.0%	.475	
EF 25.0 – 39.99	.225	.415
EF < 25.0%	.435	.631
eGFR< 60.0mls/min	.024	2.960

*Key: NYHA= New York Heart Association; BMI= body mass index; LVEF= Left ventricular ejection fraction; cGFR= estimated glomerular filteration rate; * = significant p value*

Table 3. Association of some variables with mortality

Variables	Mortality		Total no	Chi (p value)
	No no (%)	Yes no (%)		
Sex				
Male	63 (82.9)	13(17.1)	76	2.01 (0.156)
Female	76 (90.5)	8(9.5)	84	
Age group				
18-45	43 (86.0)	7(14.0)	50	3.724 (0.155)
46-65	72 (91.1)	7(89)	79	
>65	24 (77.4)	7(22.6)	31	
LOE				
Nursary and primary	36 (95.3)	7 (16.3)	43	0.513 (0.474)
Secondary and tertiary	103 (88.0)	14 (12.0)	117	
NYHA class				
Class 2	41 (95.3)	2 (4.7)	43	57.10 (<0.001)
Class 3	88 (95.7)	4 (4.3)	92	
Class 4	10 (40.0)	15 (60.0)	25	
Type of HF				
DHF	15 (100.0)	0 (0.0)	15	2.501 (0.114)
SHF	124 (85.5)	21(14.5)	145	
BMI (Kg|m^2)				
≤24.99	45 (84.9)	8 (15.1)	53	5.49 (0.064)
25-29.99	55 (82.1)	12 (17.9)	67	
≥30	39 (97.5)	1 (2.5)	40	
Haemoglobin(gm/dl)				
≥10	110 (90.9)	11 (9.1)	121	7.09 (0.008)
<10	29 (74.4)	10 (25.6)	39	
LVEF (%)				
≥40	60 (96.8)	2 (3.2)	62	8.72 (0.013)
25-39.99	57 (80.3)	14 (19.7)	71	
<25	22 (81.5)	5 (18.5)	27	
cGFR(mls/min)				
≥60	93 (90.3)	10 (9.7)	103	2.96 (0.085)
<60	46 (80.7)	11(19.3)	57	

Key: LOE=Level of education;NYHA= New York Heart Association; DHF= diastolic heart failure; SHF= systolic heart failure; BMI= body mass index; LVEF= Left ventricular ejection fraction; eGFR= estimated glomerular filteration rate; No= number; %= percent within variable

The treatment chart showed that most participants received standard treatment for heart failure as all patients received a loop diuretic on admission, 98% received either an angiotensin receptor blocker or angiotensin converting enzyme inhibitor. 80% of all participants received a mineralocortiocid receptor antagonist, 75% received low dose aspirin, 11% received warfarin 95% received digoxin. None received a beta blocker on admission but 77% were prescribed a beta blocker on discharge. Thus more than 80% of all participants received standard guideline recommended treatment for heart failure and the trend is not surprising the center being a tertiary health institution and a post graduate medical training center Table 5.

Table 4. Logistic regression analysis of some variables with mortality

	P value	Odds ratio
NYHA class 2	.000	
NYHA class 3	.001	1.90
NYHA class 4	.000	9.00
HB < 10.0 gm%	.950	1.049
EF> 40%	.018	
EF 25- 39.99%	.643	1.798
EF < 25.0%	.014	14.621

NYHA= New York Heart Association; LVEF= Left ventricular ejection fraction

Table 5. Pattern of heart failure treatment

Drug	% age of patients
Angiotensin converting Enzyme inhibitors/ Angiotensin Receptor Blocker	98%
Beta blockers	NIL
Loop diuretic	100%
Mineralocorticoid Receptor antagonist	80%
Digoxin	95
Warfarin	11%
Low dose aspirin	75%

4. DISCUSSION

The study showed that in this cohort of patients from southern Nigeria, the average age of the patients with HF was 52.49±13.89 years, thus HF affects the most productive age or people in their prime. Reduced life expectancy, poor health infrastructure and an almost epidemic explosion of cardiovascular risk factors in Sub Saharan Africa and other low income countries are contributory factors. The lower average age in our study and that of other studies emanating from Africa has been attributed to the fact that the major causes of HF in sub-Saharan Africa such as hypertension, rheumatic heart disease, idiopathic dilated cardiomyopathy and HIV related heart disease which affects mainly the young and the middle-aged. Also hypertension detection, treatment and control in Nigeria as in other African countries is generally poor, hence heart failure and other complications are expected to occur earlier. This finding is at variance with those of patients in developed countries where HF remains predominantly a disease of the elderly [27-28]. In Spain, Permanyer et al. [29] found that almost 40% of HF patients were over 80 years, and more than 70% were over 70 years of age. This is also similar to the pattern in other developed countries such as the United States of America where average age of HF patients was about 70 years [30].

The major etiology of heart failure detected in this study were hypertension, dilated cardiomyopathy and rheumatic valve disease accounting for 83.75% of all cases. Hypertension and hypertensive heart disease account for 51.25% and is the most frequent etiology and is in keeping with studies from other parts of Africa [31-32]. This may account for the non use of beta blockers in the participants during admission whereas beta blockers are a major class of drug used in developed countries where heart failure is majorly due to ischemic heart disease. Late presentation of participants to the hospital was a significant finding in this study, with 57.5% of the participants presenting in NYHA class III and 15.6% in class IV. This late presentation appears to be a common finding in African patients as studies from other investigators in the African continent show similar trend [15,33]. This late presentation at an advanced NYHA class has been shown to impacts negatively on the prognosis and outcome of heart failure participants [15]. This fact was also shown in this study where the severity of the NYHA functional class of the participants at presentation was found to be an important determinant of outcome. The late presentation of participants in this study may be attributable to lack of universal health insurance in our country as all the participants were paying out of pocket as at the time of the study.

4.1 Clinical Endpoints after 6 Months of Follow Up

In this study, 10% of the patients were lost to follow-up and all attempts at location by telephone contact or physical address was futile and the reasons were not quite clear. The address of some of the participants were nonspecific and in rural areas, out of the city where our hospital is located.

4.1.1 Rehospitalisation

The rehospitalisation rate of HF in this study was 35.6% and is quite high and unexpected as most of the patients received standard therapy for heart failure. The reason for this is not clear but several factors such as out of pocket drug purchases which make post discharge drug compliance difficult to ascertain. Also it is expected that the younger age of this cohort which means fewer co morbidities would have impacted positively on re hospitalisation but this was not so. Low quality drugs in circulation in the country may be an important cause of treatment failure which may contribute to the increased re hospitalisation rate. The determinants of re hospitalization in this study were the NYHA class at presentation, the higher NYHA [NYHA 3 AND 4] being associated with higher readmission rate, the type of heart failure (systolic heart failure), low haemoglobin level (<10 gm/l) and low eGFR (eGFR values <60 mls/min). This re hospitalisation rate is higher than figures from the United States where Ross et al. [34], using the data from Medicare, documented 30-day readmission rates after HF hospitalization of 23.0% in 2004, 23.3% in 2005, and 22.9% in 2006. Ogah et al. [35] in a recent study in the south west region of Nigeria reported a rehospitalisation rate of 12.2% and identified presence of mitral regurgitation, age ≥ 60 years, presence of tricuspid regurgitation, atrial fibrillation and Left Ventricular Ejection Fraction as factors associated with 6months rehospitalization. Thus hospitalization and high rehospitalisation rate of HF patients pose substantial burden and continues to be of great public heath significance especially in a developing economy like Nigeria.

4.1.2 Mortality

The six months [180 days] mortality in this patient cohort was 13.1% and is considered high. The contributory factors may include well known negative predictive factors in heart failure such as late presentation in advanced heart failure, low ejection fraction, co morbidity such as anaemia and raised serum creatinine. Heart failure is a progressive disease that is ultimately fatal and the presence of several co morbidities would impact negatively on outcomes and raise the mortality. The 6monhs mortality in this cohort is similar to the figures documented for hypertensive HF patients in the same institution about two decades ago where investigators reported mortality rate of 13.6% [36]. This finding thus suggests that mortality from HF in our environment has remained relatively stable despite advances in treatment modalities. This mortality rate is also comparable to the mortality of 10% reported in the northern part of Nigeria though these were not longitudinal studies [37]. It was however much lower than the 30.8% documented from South Western part of Nigeria [33] and the 35% documented in Lusaka, Zambia [38]. The high mortality rate from Western Nigeria may however be attributable to the late presentation with more than 90% of them presenting in NYHA class IV while the Zambian investigators admitted logistic and financial challenges that made it difficult to optimize patient's treatment. However Ogah et al. [35] in a recent study in the south west region of Nigeria reported a rehospitalization rate of 12.2% and mortality rate of 4.2% at 6 months of follow-up. In our cohort the identified determinants or predictors of 6months mortality were high NYHA class (Class III and IV) and low left ventricular ejection fraction (LVEF < 25%). Karaye et al. [37] in Northern Nigeria also noted the poor prognostic value of low LVEF of < 40%. Age and anaemia did not appear to be significant in determining mortality outcome. This finding appear to be at variance with the result of other studies done within and outside Africa. Falase et al. [39] reported the prognostic importance of anaemia in HF patients while Familoni et al. [15] also from Nigeria reported factors associated with poor outcome in HF patients to include anaemia, low eGFR, increased age and low haemoglobin of <10gm/dl. Nohria et al. [3] documented high NYHA class, low LVEF, advanced age, low eGFR, anaemia and other co-morbid conditions as factors that negatively affect outcome in HF patients. Using data from the sub-Saharan Africa Survey of Heart Failure (THESUS-HF), Sliwa et al. [40] also noted that the main predictors of 60-day re-admission or death were a history of malignancy and severe lung disease, admission systolic blood pressure, heart rate and signs of congestion (rales), kidney dysfunction (BUN),

anaemia, HIV positivity and echocardiographic ejection fraction.

Thus the determinants of mortality and rehospitalisation in this cohort of Nigerians is similar to findings from other parts of Nigeria and Sub Saharan Africa though some minor differences existed probably related to difference in sample size and availability of facilities for monitoring. This is not surprising since the etiology of heart failure in this region is similar and due mainly to hypertension, cardiomyopathy and rheumatic valvular heart disease.

5. CONCLUSION

As in other studies of HF patients in sub-Saharan Africa, heart failure patients in Port Harcourt, South South region of Nigeria are relatively young, being in their fifth to sixth decades of life and present in advanced NYHA functional state. The determinants of mortality were advanced NYHA class and low left ventricular ejection fraction while the determinants of re hospitalisation were advanced NYHA class, anemia, systolic heart failure and impaired renal function [low eGFR].

6. LIMITATION OF STUDY

Small sample size and high attrition rate may not reflect the true relationship between variables and rehospitalisation as well as mortality.

CONSENT

As per international standard or university standard, patient's written consent has been collected and preserved by the authors.

ETHICAL APPROVAL

As per international standard or university standard, written approval of Ethics committee has been collected and preserved by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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